REMARKS

The invention provides for, *inter alia,* bicyclic heterocycles, processes for their preparation and their use as herbicides and pharmaceutical agents. It had been unexpectedly discovered that these bicyclic heterocycles exhibit AMPDA and ADA inhibition activity, especially in plants.

Pursuant to the provisions of 37 C.F.R. §§ 1.17(a) and 1.136(a), Applicants petition the Assistant Commissioner to extend the time period for Applicants to respond to the outstanding Office Action by three (3) months, i.e., up to and including October 22, 2004. A check for $980.00 is enclosed with this paper. Applicants authorize the Director to charge any additional fee for consideration of this paper, or credit any overpayment, to Deposit Account No. 50-0320.

Claims 1-21 are pending in this application. Claims 1, 3,5 and 8 are amended and claims 18-21 are cancelled without prejudice, admission, surrender of subject matter or intention of creating estoppels as to equivalents. Support for the amendments to claims 1, 3, 5, and 8 is found in the specification and in the cancelled claims. Thus, the amendment for the definition of G in claim 1 is supported by the specification where the preferred meaning is discloses at page 3, line 25 and the amendment for the definition of G in claim 3 and 5 is supported by the specification where the preferred meaning is disclosed at page 3, line 25. The dependency of claim 8 is changed from claim 7 to claim 1. Further, the support for the more detailed definitions of Z^1, Z^2 and $R^{1\text{-}17}$ in the amended claim 1, can be found in the cancelled claim 4. Therefore, no new matter is present.

In order to advance prosecution and to achieve a reasonable compromise with the Examiner, Applicants deleted claims 18 to 21 directed to the pharmaceutical aspects of the invention. This was done in the light of the Examiner's opinion that tests on living mammalian

hosts have to be provided before any pharmaceutical claim is accepted. Applicants disagree and urge that the tests on AMPDA of calf intestine and of ADA from rabbit muscle (see biological examples B and C) provide strong support for the pharmaceutical potential of these compounds. Applicants reserve the right to pursue this subject matter in a divisional application.

It should further be emphasized that the invention relates to the inhibitors of ADA and AMPDA which were not known before the instant compounds of formula (I). The effect of the instant AMPDA inhibitors in plants is clearly shown by the Applicants (see Chapter C (Biol. Examples), sect. 1, subsect. A, and Chapter C, sect. 2 and 3). Moreover, Applicants believe that the invention discloses valuable tools, such as functional essays, which may be used by one skilled in the art for measuring the efficacies of the instant inhibitors in *vivo* and in *vitro*.

Claims 1-21 were rejected under 35 U.S.C. §112, first paragraph, for allegedly not being enabled. For the reasons that follow, Applicants respectfully assert that the specification in combination with the knowledge in the art, discloses sufficient information for assuming that instant bicyclic heterocycles have similar structural and functional activity as potent inhibitors of AMPDA. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

It is respectfully submitted that the assertions in the Office Action that undue experimentation is required to practice the instantly claimed invention are inaccurate. The Examiner is respectfully invited to review *In re Wands*, 8 U.S.P.Q. 2d 1400 (Fed. Cir. 1988), wherein the Federal Circuit stated at 1404 that:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness,

> having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted].

Against this background, determining whether undue experimentation is required to practice a claimed invention turns on weighing the factors summarized in *In re Wands*. These factors include, for example, (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples of the invention; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims; all of which must be taken into account.

Moreover, the Examiner is reminded that the first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. Whether this is achieved by illustrative examples or by broad terminology is of no importance. *In re Marzocchi, 169 U.S.P.Q. 367 (CCPA 1971)*. Applicants respectfully urge that through the description and the data presented in the example, Applicant have met the standard. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Contrary to the Examiner's allegations, Applicants urge that although formula (I) encompasses a large number of individual compounds the structure of the compounds is rather similar from the structural elements combined. The compounds have a core structure which is common to all compounds of formula (I), namely the bicyclic heterocyclic system linked to a hydrocarbon bridge which in turn is substituted by very polar functional groups.

Moreover, the examples show a similar effect of the compounds even if the group G-L is varied widely (see different definitions of A and G-L in the compounds 1-1, 12-1, 21-1, 21-3, 22-2, 28-1, 44-1 and 159-3). Furthermore, the tables provide even more structurally similar examples and thus provide guidance for the person skilled in the art to make other compounds similar to those having already shown a specific enzyme inhibiting effect. Applicants urge that in view of the variation of structural elements in the existing biological examples and in view of the structural similarities of these examples, a skilled artisan would have sufficient reasons to believe that other variation within the claimed group of compounds would result in the inhibiting effects too and would not require additional experimentation to deduce the function of these compounds.

Additionally, the group of heterocyclic rings involved in the basic core of formula (I) is rather limited and some of the heterocyclic systems are even tautomers or stereoisomers of other heterocyclic systems.

Thus, applying *Wands*, the following, *inter alia*, is clear: the quantity of experimentation necessary to practice the invention is low; the amount of guidance in the specification is high; the nature of the invention is not such that "an inordinate amount of experimentation" is required; the relative skill of those in the art is high; the art is predictable; and the breadth of the claims is narrow. Thus, and contrary to the allegations in the Office Action, undue experimentation would not be necessary to practice the instantly claimed invention.

Consequently, reconsideration and withdrawal of the Section 112, first paragraph, rejection for alleged lack of enablement are respectfully requested.

Claims 1-9, 11, 14 and 18-21 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite. In view of the amendments to claims 1, 3, 5 and 8, cancellation of

claims 4 and remarks submitted below, Applicants request the reconsideration and withdrawal of the rejections.

As to **claim 1,** lines 54-55, Applicants believe that the definition includes the formation of cyclic rings by replacing a saturated bond in L with a bond forming the bridge. Examples for such cyclic formation is shown e. g. as examples 58-1 or 105-1. Applicants also disagree that atom "N" cannot exist as a linking element because the linking group which contains the N-atom is a group within the definition of L where a saturated bond is replaced with the bond forming the bridge. The group within L having a nitrogen atom is normally amino. In case of a primary amino group the linking group would the be -NH-, i. e. the third valence of the N-atom is automatically saturated with hydrogen, a consequence of the definition of L.

As to **claim 1** lines 56-58, Applicants urge that definition is a more functional one, i. e. Z^1, Z^2 the radical of an inorganic or organic oxgen acid of the formula Z^1-OH or Z^2-OH. This definition is found in the specification at page 13 last paragaraph to page 14 first paragraph, and furthermore by the more preferred definitions of Z^1 and Z^2 as set forth at page 19 of the specification. Therefore, Applicants believe that the term radical of an oxygen acid well describes the similarities between the polar groups. However, in order to advance prosecution and to achieve a compromise with the Examiner, claim 1 was amended to further define definitions Z^1 and Z^2 more precisely.

As to **claim 1** lines 73-74, Applicants agree with the Examiner that heterocyclyl is a radical derived from a heterocyclic ring. However, the shortened term heterocyclic ring is often used in the art for the respective radical. For instance, this is the case when a general radical symbol R is defined as a heterocyclic ring. In this case, it is clear that R means the radical of the heterocyclic ring because the position of R in the formula indicates already the status of a

radical. Further, in the definition at page 11, first paragraph, the distinction between heterocyclic radical or ring is not made specifically and has to be taken from the context. A heterocyclic ring can be in a radical or in a heterocyclic compound in principle. Thus Applicants urge that the use of the term" heterocyclic" is appropriate in this case and this rejection should be reconsidered and withdrawn.

Additionally, as to **claim 1** lines 73-74, in order to advance prosecution, Applicants amended claim 1 to limit the number of ring atoms and heteroatoms.

Applicants urge that rejections as to claim 4 are moot in view of cancellation of claim 4.

As to **claim 8** line 8, Applicants urge that the definition is clear as the functional term "Z" is a precursor of the radical G-L" and is further illustrated in the description e. g. at page 30, lines 1 to 26. The possible reactions are derivatization reactions customary to persons skilled in the art and determined by the synthethic goal G-L. Particularly, emphasis is given there e.g. to customary protection groups for hydroxyl or amino groups. Thus, Applicants believe that one skilled in the art would know enough synthetic ways to follow this general pattern. An important step lies in the method wherein the reduction of the bicyclic system is effected on a compound having a group Z instead of the different group G-L at the respective position rather than in the particular reaction from the precursor to the group G-L. Moreover, the radical Z is defined by the final group G-L to which it has to be transformed. Applicants, thus, do not believe that it is necessary to define a functional term structurally.

As to **claims 8, 9 and 11**, Applicants believe that the terms objected to are defined sufficiently in the description. Thus, with respect to claim 8, the functional term Z used was already discussed above. With respect to the term "modifying" and the like mentioned, such as cyclizing, it has to be noted that the specific modification steps are known to a person skilled in

the art of chemistry and are not a specific contribution according to the invention which, however, is in the structure of the final product. The process gives sufficient hints how to make the compounds. It is further urged that specifying the process claims with respect to the functional terms would limit the scope of the process arbitrary. As far as the process of claim 8 is concerned the invention is in the preparation of novel final products of claim 7. Therefore, the process can be an analogous process and should be considered patentable.

It is also urged that the definition of G-L is not incomplete as alleged by the Examiner. Therefore, the process claims are also not incomplete. The processes of claims 9 and 11 are additionally based on separate inventive merit (independent from the final novel products of claim 7), as discussed previously and in the description.

Claims 7 and 18-20 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by the Duffy et al, ("Duffy"), Gewald et al "Gewald", and Milne et al "Milne". In view of the amendments to claims, cancellation of claims 18-21 and remarks presented below, Applicants respectfully request reconsideration and withdrawal of the rejection. Moreover, in view of the amendments to claim 1, Duffy and Gewald do not teach instantly claimed bicyclic heterocycles, and thus these references cannot anticipate the present claims and the withdrawal of the rejection is requested.

With respect to Duffy, Applicants urge that compound 5a (page 2458, col. 1, Scheme 2) differs from the instant compounds of formula (I) such that in Duffy, the radical CO_2Et attached directly to a bicyclic system whereas instant compounds of formula (I) need a bridge L there (e. g. at least a C_4-chain or a ring). Applicants respectfully point out that in view of the amendment of claim 1 and respective subclaims, Duffy does teach instant bicyclic heterocycles and thus cannot anticipate the present claims.

With respect to Gewald, (see page 1537, compound 9), the compound 9, referred to by the Examiner, exhibits an oxo group attached to the six-membered ring of the bicyclic system. This is in contrast to the compounds of the present invention wherein the oxo group is necessary to have a hydrogen as substituent. Moreover, the other radicals X of Gewald do not teach the instant compounds of the formula (I) either. Accordingly, Gewald does not teach the instant instant bicyclic heterocycles and thus cannot anticipate the present claims.

In view of the cancellation of claims 18-21, the 35 U.S.C. §102(b) rejection over Milne is moot and should be withdrawn.

Accordingly, in view of the foregoing, reconsideration of all rejections in this application is requested and favorable action is solicited.

Respectfully submitted,

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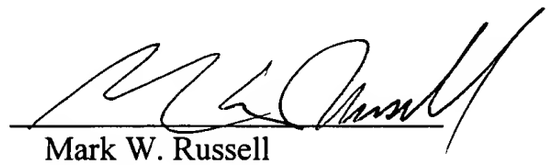
By: 

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